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**Primed mesenchymal stem cells package exosomes with metabolites associated with immunomodulation.**

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**Authors:** Megan R Showalter, Benjamin Wancewicz, Oliver Fiehn, Joehleen A Archard, Shannon Clayton, Joseph Wagner, Peter Deng, Julian Halmai, Kyle D Fink, Gerhard Bauer, Brian Fury, Nicholas H Perotti, Michelle Apperson, Janelle Butters, Peter Belafsky, Gregory Farwell, Maggie Kuhn, Jan A Nolta, Johnathon D Anderson

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**Public Summary:**

Mesenchymal stem cell (MSC) based therapies are currently being evaluated as a putative therapeutic in numerous human clinical trials. Recent reports have established that exosomes mediate much of the therapeutic properties of MSCs. Exosomes are nanovesicles which mediate intercellular communication, transmitting signals between cells which regulate a diverse range of biological processes. MSC-derived exosomes are packaged with numerous types of proteins and RNAs, however, their metabolomic and lipidomic profiles to date have not been well characterized. We previously reported that MSCs, in response to priming culture conditions that mimic the in vivo microenvironmental niche, substantially modulate cellular signaling and significantly increase the secretion of exosomes. Here we report that MSCs exposed to such priming conditions undergo glycolytic reprogramming, which homogenizes MSCs' metabolomic profile. In addition, we establish that exosomes derive from primed MSCs are packaged with numerous metabolites that have been directly associated with immunomodulation, including M2 macrophage polarization and regulatory T lymphocyte induction.

**Scientific Abstract:**

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